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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,228	10/30/2003	Yusuke Nakamura	56801 DIV (46342)	7445

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EDWARDS & ANGELL, LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 04/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/698,228	NAKAMURA ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *19-23* is/are allowed.

6)☒ Claim(s) *24-34* is/are rejected.

7)☒ Claim(s) *26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 October 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response, on February 14, 2006 to the First Action on the Merits of this case mailed November 15, 2005, is acknowledged. It is acknowledged that applicants have amended Claims 24 and 25 and added Claims 27-34. Claims 19-34 are pending and are hereby considered.

Drawings-Objections

Figures 1-3, discloses sequence(s) that are not identified by a sequence identifier number (SEQ ID NO:). The sequence rules embrace all nucleotide sequences with ten or more bases and all amino acid sequences with four or more amino acids. Said sequences must be disclosed in a sequence listing and identified by a specific SEQ ID NO: (MPEP 2421.02). 37 CFR 1.821(d) requires the use of the assigned sequence identifier number in all instances where the description or claims of a patent application discuss sequences, regardless of whether a given sequence is also embedded in the text of the description or claims of an application. Applicant is required to correct the figures, to identify all of the sequences disclosed therein by sequence identifier numbers.

Figures 1-3 are objected to for comprising a single sequence, which should be presented in a single figure and labeled panels (A)-(C). The drawing set should be corrected to reflect the correct number of figures. The specification should also be corrected in order to refer to the correct, properly numbered, figure.

Abstract-Objections

The Abstract is objected to for being a single, run-on sentence.

Specification-Objections

The specification at page 83 discloses sequence(s) that are not identified by a sequence identifier number (SEQ ID NO:). The sequence rules embrace all nucleotide sequences with ten or more bases and all amino acid sequences with four or more amino acids. Said sequences must be disclosed in a sequence listing and identified by a specific SEQ ID NO: (MPEP 2421.02). 37 CFR 1.821(d) requires the use of the assigned sequence identifier number in all instances where the description or claims of a patent application discuss sequences, regardless of whether a given sequence is also embedded in the text of the description or claims of an application. Applicant is required to correct the specification, to identify all of the sequences disclosed therein by sequence identifier numbers.

Claims-Objections

Claim 26 is objected to for the phrase "the nucleic acid according to claim 19", which is improper antecedent usage. Said phrase should be corrected to "the nucleic acid molecule according to claim 19".

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27, 28, and 33-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 27 is indefinite in the recitation of "hybridizes under stringent conditions" as this term is unclear absent a statement of the conditions under which the hybridization reaction is preformed. Nucleic acids that will hybridize under some hybridization

conditions, will not necessarily hybridize under different conditions. The hybridization conditions described on page 23 are only exemplary and do not define the conditions recited in Claim 27. Thus, Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Since, Claims 28 and 33-34 are dependent on Claim 27, said claims are also rejected under 35 U.S.C. 112, second paragraph, for the same reasons.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 27-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the isolated polynucleotides of SEQ ID NO: 2 and 12, does not reasonably provide enablement for any polynucleotide that (i) hybridizes to SEQ ID NO: 2 or 12, (ii) has at least 90% identity with SEQ ID NO: 2 or 12, or (iii) has at least 95% identity with SEQ ID NO: 2 or 12, wherein the polynucleotide encodes a protein with any or no activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to:

(1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 27 and 28 are so broad as to encompass any polynucleotide that hybridizes to SEQ ID NO: 2 or 12, wherein the polynucleotide encodes a protein with any or no activity. Claims 29 and 31 are so broad as to encompass any polynucleotide that has at least 90% identity with SEQ ID NO: 2 or 12, wherein the polynucleotide encodes a protein with any or no activity. Claims 30 and 32 are so broad as to encompass any polynucleotide that has at least 95% identity with SEQ ID NO: 2 or 12, wherein the polynucleotide encodes a protein with any or no activity. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of SEQ ID NO: 1 and the nucleotide sequences of SEQ ID NO: 2 and 12.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims.

Furthermore, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable (Galye et al, 1993; Whisstock et al, 2003). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of Claims 27 and 28 which, encompasses all polynucleotide sequences that hybridizes to SEQ ID NO: 2 or 12, wherein the polynucleotide encodes a protein with any or no activity. The specification also does not support the broad scope of Claims 29 and 31, which encompasses all polynucleotide sequences that have at least 90% identity with SEQ ID NO: 2 or 12, wherein the polynucleotide encodes a protein with any or no activity. The specification also does not support the broad scope of Claims 30 and 32, which encompasses all polynucleotide sequences that have at least 95% identity with SEQ ID NO: 2 or 12, wherein the polynucleotide encodes a protein with any or no activity. The specification does not support the broad scope of Claims 28-32 because the specification does not establish: (A) the activity of all polypeptides encoded by the recited polynucleotides; (B) regions of the protein structure which may be modified without effecting the desired activity; (C) the general tolerance of the desired activity to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Since Claims 33-34 further recite vectors, host cells, and pharmaceutical compositions comprising the polynucleotides of Claims 37-32, Claims 33-34 are also rejected under 35 U.S.C. 112 first paragraph due to lack of enablement for the same reasons discussed above.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of polynucleotides encoding polypeptides with an enormous number of amino acid modifications of the polypeptide of SEQ ID NO: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 24, 25, and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated host cell transformed with the synthetic nucleic acid molecules does not reasonably provide enablement for a transformed host cell within a multicellular organism that has been transformed with nucleic acid molecules. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 24 and 34 are so broad as to encompass host cells transformed with specific nucleic acids, including cells in *in vitro* culture as well as cells within any multicellular organism. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of host cells broadly encompassed by the

claims. While methods for transforming cells *in vitro* are well known in the art, methods for successfully transforming cells within complex multicellular organisms are not routine and are highly unpredictable. Furthermore, methods for producing a successfully transformed cell within one multicellular organism are unlikely to be applicable to transformation of other types of multicellular organisms as multicellular organisms vary widely. However, in this case the disclosure is limited to only host cells *in vitro*. Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including the use of host cells within a multicellular organism for the production of polypeptide. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, expression of genes in a particular host cell and having the desired biological characteristics is unpredictable the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). Claim 25, as dependent from Claim 24, is rejected under 35 U.S.C. 112, first paragraph, for the same reasons. It is suggested that applicants limit the claims to "An isolated transformed cell ...".

Claim 26 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a polynucleotide encoding the polypeptide of SEQ ID NO: 1, does not reasonably provide enablement for a pharmaceutical composition comprising said polynucleotide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims without undue experimentation.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The factors most relevant to this rejection are the unpredictability in the art, the amount of experimentation required, and the amount of direction or guidance presented. The term "pharmaceutical" implies treatment of a disease. It is acknowledged that the specification asserts that a pharmaceutical composition comprising a polynucleotide encoding SEQ ID NO: 1 can be used for the treatment of cancer (pg 90). It is also acknowledged that the specification discloses that expression of a polynucleotide encoding SEQ ID NO: 1 in host cells increases DNA repair in response to UV irradiation (Example 4). However, no evidence of a link between the effects of the polynucleotide encoding SEQ ID NO: 1 in cultured cells and any specific disease is provided. It is unpredictable what diseases can be effectively treated using a "pharmaceutical composition" comprising a polynucleotide encoding SEQ ID NO: 1. Neither the specification nor the prior art provide sufficient guidance as to what specific diseases, including any specific cancers, could be successfully treated by administering a "pharmaceutical composition" comprising the polynucleotide encoding SEQ ID NO: 1. Furthermore, attempting to identify a disease treatable using such a "pharmaceutical composition" would constitute undue experimentation and the success for treatment of any disease, including any cancer, is unpredictable (Fernandez-Trigo et al, 1995). While methods for testing a pharmaceutical compositions' usefulness in treating some diseases are known, such methods are not trivial. Furthermore, the specification fails to provide guidance as what, in addition to the polynucleotide of SEQ ID NO: 1, the composition should comprise. Making and testing an infinite number of compositions to find one that is effective against any of the large number of known diseases would clearly constitute undue

experimentation. Therefore, the specification fails to enable one of ordinary skill in the art how to make and/or use the "pharmaceutical composition" encompassed by the claim.

Written Description

Claims 27-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Inventors, at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of nucleic acid molecules having the limitations of hybridizing to SEQ ID NO: 2 or SEQ ID NO: 12 or having at least 90% or at least 95% identity with SEQ ID NO: 2 or 12. The specification does not contain any disclosure of the function of all nucleic acid sequences that hybridize to SEQ ID NO: 2 or SEQ ID NO: 12 or that have at least 90% or at least 95% identity with SEQ ID NO: 2 or 12. The genus of polynucleotides that comprise these above nucleic acid molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated nucleic acid molecules are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses the function of only two species of the claimed genus, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 24 and 34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Inventors, at the time the application was filed, had possession

of the claimed invention. These claims are directed to a genus of host cells, within any multicellular organism, wherein the host cell is transformed with specific nucleic acids. The specification does not contain any disclosure of the function of all transformed multicellular organisms. The genus of host cells, within any multicellular organism, that comprise these above recombinant organisms is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated host cells and organisms are encompassed within the scope of these claims. The specification discloses the function of no representative species of the claimed genus, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Allowable Subject Matter

Claims 19-23 recite allowable subject matter.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Regarding filing an Appeal, Applicants are referred to the Official Gazette Notice published July 12, 2005 describing the Pre-Appeal Brief Review Program.

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHERIDAN SWOPE, PH.D.
PRIMARY EXAMINER